REMARKS

In this Amendment, claims 107, 111, 112 and 114 have been amended, and claims 1-106, 108, 113 and 115-153 have been canceled without prejudice or disclaimer. In addition, claims 154-217 are newly presented. Accordingly, the currently pending claims are now claims 107, 109-112, 114 and 154-217. It is submitted that no new matter has been added by virtue of the amended and new claims, which are supported by the claims and the application disclosure as originally filed.

Support for Amended and New Claims

Support for amended claim 107 is found in the disclosures of both priority applications (i.e., U.S. Serial Nos. 60/083,917 ("the '917 application"), and 09/302,896, ("the '896 application")), as well as in the instant application. The instant application specifically refers to the muscle-derived cell isolation method of the '896 application, for example, on page 28, lines 29-31 to page 29, lines 1-23 of the instant application; this isolation method is incorporated by reference in the instant application (See, e.g., page 51). The '896 application contains the same pertinent disclosure as does the '917 application at page 81, Example 11.

Additionally, support for new claims 154 and 155, directed to methods involving muscle-derived cells isolated by Applicants' claimed method for augmenting or bulking esophageal muscle tissue, is found in prior claims 119 and 133. Support for new claim 156 is found in prior claim 140. Support for new claim 157 is found in prior claims 117 and 131. Support for new claim 158 is found in the instant specification, for example, at page 18, lines 4-5. Support for new claim 159 is found in prior claims 118 and 132; and support for new claim 160 is found in the instant specification, *inter alia*, on page 18, lines 22-25. Support for new claims 161 and 162, directed to methods involving augmenting or bulking gastroesophageal muscle tissue is found in prior claims 120, 134 and 141.

Support for new claims 163 and 164, directed to methods involving muscle-derived cells isolated by Applicants' claimed method for augmenting or bulking sphincter muscle tissue, is found in prior claims 121 and 135. Support for new claim 165 is found in prior claim 142. Support for new claim 166 is found in prior claims 117 and 131. Support for new claim

167 is found in the instant specification, for example, at page 18, lines 4-5. Support for new claim 168 is found in prior claims 118 and 132; and support for new claim 169 is found in the instant specification, *inter alia*, on page 18, lines 22-25.

Support for new claims 170 and 171, directed to methods involving muscle-derived cells isolated by Applicants' claimed method for augmenting or bulking bladder muscle tissue, is found in prior claim 124. Support for new claim 172 is found in prior claim 145. Support for new claim 173 is found in prior claims 123 and 144. Support for new claim 174 is found in prior claims 117 and 131. Support for new claim 175 is found in the instant specification, for example, at page 18, lines 4-5. Support for new claim 176 is found in prior claims 118 and 132; and support for new claim 177 is found in the instant specification, *inter alia*, on page 18, lines 22-25.

Support for new claims 178, 179, 184 and 185, directed to methods involving muscle-derived cells isolated by Applicants' claimed method for augmenting or bulking muscle tissue to ameliorate a cosmetic or aesthetic defect, or a cutaneous depression, wound, or fissure opening is found in prior claims 125 and 126, and in the instant specification, *inter alia*, on page 20, lines 20-31 to page 21, lines 1-6. Support for new claims 180 and 186 is found in prior claims 117 and 131. Support for new claims 181 and 187 is found in the instant specification, for example, at page 18, lines 4-5, and in the instant specification, *inter alia*, at page 18, lines 25-30 and at page 21, lines 1-2. Support for new claims 182 and 188 is found in prior claims 118 and 132; and support for new claims 183 and 189 is found in the instant specification, *inter alia*, on page 18, lines 22-25.

Support for new claims 190 and 191, directed to methods involving isolated, desmin-expressing, skeletal muscle-derived progenitor cells for augmenting or bulking esophageal muscle tissue is found in pending and prior claims 119 and 133, and in the instant specification, *inter alia,* on page 6, lines 22 through to page 7, lines 1-14, for example. Support for new claim 192 is found in prior claim 140. Support for new claim 193 is found in prior claims 117 and 131. Support for new claim 194 is found in the instant specification, for example, at page 18, lines 4-5. Support for new claim 195 is found in the instant specification,

inter alia, on page 18, lines 22-25. Support for new claim 196, directed to augmenting or bulking gastroesophageal muscle tissue is found in pending and prior claims 120 and 134.

Support for new claims 197 and 198, directed to methods involving isolated, desmin-expressing, skeletal muscle-derived progenitor cells for ameliorating a cosmetic or aesthetic defect or a cutaneous depression, wound, or fissure opening is found in prior claims 125 and 126 and in the instant specification, *inter alia*, on page 20, lines 20-31 to page 21, lines 1-6. Support for new claim 199 is found in the instant specification, for example, at page 18, lines 4-5. Support for new claim 200 is found in the instant specification, *inter alia*, on page 18, lines 22-25.

Support for new claims 201 and 202, directed to methods involving isolated, desmin-expressing, skeletal muscle-derived progenitor cells for augmenting or bulking sphincter muscle tissue is found in pending and prior claims 121 and 135. Support for new claim 203 is found in prior claims 142 and 143. Support for new claim 204 is found in the instant specification, for example, at page 18, lines 4-5; and support for new claim 205 is found in the instant specification, *inter alia*, on page 18, lines 22-25.

Support for new claims 206, 207 and 209, directed to methods involving isolated, desmin-expressing, skeletal muscle-derived progenitor cells for augmenting or bulking bladder or ureteral-bladder muscle tissue is found in pending and prior claims 123, 124 and 144. Support for new claim 208 is found in prior claim 145. Support for new claim 210 is found in the instant specification, for example, at page 18, lines 4-5. Support for new claim 211 is found in the instant specification, *inter alia*, on page 18, lines 22-25.

Support for new claims 212-215, directed to methods involving isolated, desmin-expressing, skeletal muscle-derived progenitor cells for augmenting or bulking muscle tissue comprising one or more of a cutaneous depression, wound, fissure, or opening, is found in the instant specification, *inter alia*, on page 20, lines 20-31 to page 21, lines 1-6.

Support for new claims 216 and 217 is found in the priority applications and throughout the specification of the instant application, for example, at page 20, line 20 through to page 21,

lines 1-6; at page 28, lines 30-31, bridging page 29, lines 1-23; at page 19, line 28 to page 23, line 10, in Figs. 1-6; and in Examples 1-6.

Allowable Claims

Applicants note that the Examiner has indicated that claims 107 and 109-112 are in condition for allowance because they are free of the prior art of record. (04/29/2004 Office Action, page 33). In addition, the Examiner has stated that claims 119, 120, 125, 126 and 133-136 are free of the art of record and would be allowable if rewritten in independent form including the limitations of the base claims and any intervening claims. (*Id.*). Applicants respectfully submit that the newly-presented claims describe inventive methods that are both new and useful in the art, and that the newly claimed methods should also be deemed allowable as they are closely based on claimed subject matter that has been stated to be free of the art and allowable by the Examiner. Thus, it is respectfully submitted that the amended and new claims are presented in form for allowance.

Priority

The Examiner has alleged that the provisional application (USSN 60/083,917) and application USSN 09/302,896 ("the '896 application"), to which the instant application claims priority under 35 U.S.C. §§119(e) and 120, respectively, fail to provide adequate support under 35 U.S.C. §112 for claims 107-112 of the application, because the priority applications disclose in a step of the MDC isolation method that the muscle-derived cells are transferred when approximately 15-20% of the cells from the cell suspension have adhered to the first container, while the instant application discloses in a step of the isolation method that the muscle-derived cells are transferred when approximately 30-40% of the cells from the cell suspension have adhered to the first container.

Because the instant application claims priority to the foregoing prior applications, which are incorporated by reference in the instant application, Applicants have amended claim 107 to reflect that in the claimed MDC isolation method, non-adherent cells are plated in a second container when approximately 15 to 40% of the cells from the cell suspension have adhered to the first container. Accordingly, claim 107 finds support in the disclosures of both

of the priority applications, as well as in the instant application. The instant application specifically refers to the muscle-derived cell isolation method of the '896 application (See, e.g., page 28, lines 29-31 to page 29, lines 1-23 of the instant application), which is incorporated by reference in the instant application (See, e.g., page 51). The '896 application contains the same pertinent disclosure as does the provisional application at page 81, Example 11. Accordingly, Applicants submit that presently amended claim 107 and its currently pending dependent claims 109-112 are supported by the disclosures of the priority applications and the instant application.

Objection to the Disclosure

The disclosure has been objected to because of informalities reflected by a lack of the present status of the U.S. applications disclosed therein. Applicants have amended the specification to include the presently known status of the relevant patent applications. Accordingly, the objection to the disclosure has been overcome

Objection to the Claims

Claim 107 and its dependent claims 108-115 have been objected to for containing multiple periods. Applicants have amended claim 107 to remove extraneous periods. Accordingly, the objection to these claims is moot.

In the Remarks below, the Office Action dated April 29, 2004 has been considered as if it pertains to the newly presented claims 154-217. Thus, this Amendment is responsive to the April 29, 2004 Office Action as if it applies to the new claims.

The claims fulfill the requirements of 35 U.S.C. §112, first paragraph

Claim 108 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Without acquiescing as to the propriety of this rejection, claim 108 is canceled without prejudice or disclaimer herein. Thus, the rejection of claim 108 under §112, first paragraph, is moot.

Claims 108, 127-129 and 137-153 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to provide enablement for "a genus of isolated muscle-derived progenitor cells express[ing] desmin and ... also express[ing] a cell marker selected from the group consisting of CD34, Bcl-2, Sca-1, and Flk-1; and using the cells in a genus of therapeutic methods ... ." (4/29/2004 Office Action, page 4).

Applicants respectfully disagree and point out that the presently claimed invention is directed to methods of augmenting or bulking particular types of muscle tissue, e.g., esophageal, gastroesophageal, bladder, or sphincter, using muscle derived cells isolated according to Applicants' claimed method. In addition, the claimed invention is directed to inventive methods of augmenting or bulking the aforementioned particular types of muscle tissue using isolated, desmin-expressing, skeletal muscle-derived progenitor cells. It is submitted that the claims as presented herein are enabled by Applicants' disclosure.

The Examiner has recognized that Applicants' specification is enabling for augmenting or bulking particular types of smooth and skeletal muscle tissues. (04/29/2004 Office Action, pages 14 and 33). Applicants respectfully point out that the present claims are directed to augmenting or bulking of particular types of muscle tissues and are supported by the specification, which shows the persistence of Applicants' isolated MDCs following injection. For example, Fig. 1 and its related disclosure demonstrate injection and subcutaneous persistence of MDCs in abdominal muscle wall versus collagen injection; Fig. 2 demonstrates the injection of MDCs into esophageal and sphincter tissue; Fig. 3 demonstrates the injection of MDCs in ureteral-bladder tissue; Figs. 4 and 5 demonstrate the injection of MDCs in cryodamaged bladder tissue and the differentiation of the injected cells over time in the bladder tissue environment. Fig. 16 further demonstrates that MDCs that are provided in a collagen sponge matrix can ameliorate, or enhance repair of, a bone-related injury.

Additionally, published experiments based on Applicants' teachings and disclosure have shown that isolated MDCs can be used in methods as described in the instant application to augment, bulk and ameliorate muscle tissues. (See, Applicants' July 28, 2003 Amendment, of record, at pages 10-11 and 15; See also, Declaration of M. Chancellor, dated 11/2002, of record). Thus, it is submitted that Applicants have enabled the use of isolated skeletal MDCs

in augmenting or bulking different types of muscle tissue, or in ameliorating an injury in a variety of particular types of muscle tissues.

Applicants respectfully disagree with the Examiner's assertion that the as-filed specification fails to provide a teaching of appropriate doses of MDCs for use in the claimed methods. (04/29/2004 Office Action, page 16). Applicants respectfully direct the Examiner to such teaching as found in the instant specification, *inter alia*, on page 18, lines 1-12 and on page 20, lines 9-19. Moreover, Applicants point out that dosing for particular routes of administration is known by the skilled practitioner in the art.

The Examiner has stated that the specification enables MDCs in a method of augmenting or bulking smooth or skeletal muscle tissue in a recipient. (04/29/2004 Office Action, page 14). Applicants' specification plainly discloses, teaches and exemplifies how to isolate and obtain a population of desmin-expressing muscle-derived cells that are sustainable in a tissue into which the cells are injected. (See, for example, the instant specification at page 14, lines 25-30; pages 28-29; and pages 32-37, Examples 2-6). Applicants further provide novel methods for the use of isolated, desmin-expressing, skeletal muscle-derived cells in augmenting or bulking several distinct types of muscle tissues. Applicants have provided a number of working examples showing that the described MDCs can be used in methods, such as those presently claimed. (See, e.g., pages 32-37, Examples 2-6). That those skilled in the art can and have reproduced and utilized Applicants' teachings and described methods, as mentioned above, offers additional support that the presently claimed invention is not of undue breadth and is readily understood and practiced by the skilled practitioner in the art.

Applicants have further employed reputable animal models to show that isolated, desmin-expressing skeletal muscle-derived cells can be administered to a living recipient. Following administration, the cells proliferate and survive in muscle tissue. (See, e.g., Figs. 1A-F, 2A/B, 3A/B, 4A/B, 5A-I, pages 7-10 of the instant specification). In the case of cryodamaged bladder, for example, the injected MDCs ameliorate the muscle tissue defect. (See, e.g., Figs. 4A/B and 5A-I). The animal studies described in Applicants' examples reveal that MDCs obtained from skeletal muscle survive and develop in smooth muscle tissue following introduction or transplantation into the recipient animal tissue. As shown by the

above Figures and described in Applicants' disclosure, the MDCs also survived and assimilated as muscle tissue cells (e.g., formed myofibers) post-injection, for days and weeks or longer. (See, for example, Figs. 5A-I and the description thereof at pages 9-10 of the instant specification).

Based on Applicants' specification, exemplification, and evidence, it is submitted that Applicants have indeed provided reasonable detail and exemplification to enable the public, and those having skill in the art, to carry out the presently claimed invention without excessive or undue experimentation. In view of the foregoing, Applicants respectfully submit that one having skill in the pertinent art could employ routine skill, and would not have to undergo undue experimentation, to obtain isolated, desmin-expressing, MDCs as described by Applicants. (See, e.g., Example 1, page 29, lines 24-27 to page 30, Table 1). Also, without undue experimentation, the skilled practitioner can further use such MDCs in the claimed methods for augmenting or bulking the particular types of muscle tissue, as is clearly described and exemplified in the instant specification.

Based on the above discussion, Applicants respectfully submit that all of the presently pending claims satisfy the requirements of 35 U.S.C. §112, first paragraph. Accordingly, reconsideration and withdrawal of the §112, first paragraph rejection are respectfully requested.

The claims fulfill the requirements of 35 U.S.C. §112, second paragraph

Claim 128 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. According to the Examiner, claim 128 recites "a condition of the lumen", which has insufficient antecedent basis. Without acquiescing to the propriety of this rejection, Applicants have canceled claim 128 without prejudice or disclaimer, thus mooting the rejection. Withdrawal of the rejection is respectfully requested.

The claims fulfill the requirements of 35 U.S.C. § 102

Claim 113 stands rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Anderson et al. (U.S. Patent No. 6,001,654), ("the '654 patent"). The rejection is moot in view of the cancellation of this claim. Withdrawal of the rejection is respectfully requested.

Claim 113 also stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Huard et al. (IDS, 1994, Muscle & Nerve, pp. 224-234) as evident by Rando et al. (*J. Cell Biol.*, 125:1275-1287, 1994, IDS). The rejection is moot in view of the cancellation of this claim. Withdrawal of the rejection is respectfully requested.

Claims 113, 114 and 115 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Rando et al. (*J. Cell Biol.*, 125:1275-1287, 1994, IDS), ("Rando").

The rejection is moot in view of the cancellation of claims 113 and 115. Further, this rejection is overcome in view of the amendment of claim 114 to depend from claim 107, which has been deemed allowable and free from the art of record by the Examiner, (See, 04/29/2004 Office Action, page 33). With regard to the present claims, Rando teaches neither Applicants' claimed method of isolating a population of muscle-derived cells nor the use of these cells in the claimed methods of augmenting or bulking muscle tissue. Rando also does not teach Applicants' novel, claimed methods involving isolated MDCs for augmenting or bulking particularly-described types of muscle tissues following injection. Accordingly, withdrawal of this rejection under 35 U.S.C. § 102(b) is respectfully requested.

Claims 113, 114, 115, 130 and 131 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Arcila et al. (*J. Neurobiol.*, 33:185-198, 1997, IDS).

Applicants submit that this rejection has been overcome in view of the cancellation of claims 113, 115, 130 and 131, and the amendment of claim 114 to depend from claim 107, which has been deemed allowable and free from the art of record by the Examiner. In addition, the claims as currently presented are not anticipated by Arcila et al., which does not

teach Applicants' novel, claimed methods involving isolated MDCs for augmenting or bulking particularly-described types of muscle tissues following injection. Accordingly, withdrawal of this rejection under 35 U.S.C. § 102(a) is respectfully requested.

Claims 113-115, 130-132 and 147-149 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Law et al. (U.S. Patent No. 5,130,141, IDS).

Applicants submit that the cancellation without prejudice of claims 113, 115, 130-132 and 147-149, and the amendment of claim 114 to depend from claim 107, which has been deemed allowable and free from the art of record by the Examiner, overcome the rejection of these claims by the Lee et al. patent. In addition, the claims as currently presented are not anticipated by Lee et al., which does not teach Applicants' novel, claimed methods involving MDCs for augmenting or bulking particularly-described types of muscle tissues following injection. Accordingly, withdrawal of this rejection under 35 U.S.C. § 102(a) is respectfully requested.

Double Patenting

Claims 116-118, 121-124, 130, 137, 144 and 145 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 196, 199, 212, 215 and 244 of co-pending application U.S. Serial No. 09/302,896. According to the Examiner, the conflicting claims are not identical, but are considered to be obvious variants of one another.

Applicants respectfully request that this rejection be held in abeyance until the claims in the instant application have been deemed to be allowable, at which time, Applicants will file an appropriate terminal disclaimer.

CONCLUSION

Applicants respectfully submit that the application is now in condition for allowance. An action progressing this application to issue is courteously urged.

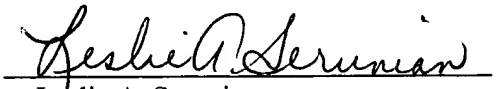
Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this amendment and response, or during the pendancy of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**, Reference no. **28682-510-CIP**, Customer Number: **35437**.

If the Examiner believes that it would be helpful to discuss the application to advance the prosecution of the application and claims to allowance, he is respectfully requested to telephone applicants' undersigned representative at (212) 692-6742 and is assured of full cooperation in this effort.

Respectfully submitted,

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.

Date: September 27, 2004

By: 
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